REMARKS/ARGUMENTS

Favorable reconsideration of this application, as presently amended and in light of the following discussion, is respectfully requested.

Claims 28-38 are presently pending in this application, Claims 16 and 18-27 having been canceled by the present amendment.

In the outstanding Office Action, Claim 16 was rejected under 35 U.S.C. §102(e) as being anticipated by Bisgaier et al. (U.S. Publication 2004/0038891); and Claims 16 and 18-38 were rejected under 35 U.S.C. §103(a) as being unpatentable over Bisgaier et al. as evidenced by Welch et al. (U.S. Publication 2006/0257866).

Briefly recapitulating, Claim 28 is directed to a method for improving prognosis, neurological symptoms, or motor dysfunction of a disease resulting from cerebral infarction, and it recites "administering an effective amount of paraoxonase to improve one of prognosis, neurological symptoms and motor dysfunction of a disease resulting from cerebral infarction to a patient in need thereof."

Paraoxonase (PON) is a Ca^{2+}-dependent glycoprotein having a molecular weight of about 45 kDa which exists as one of protein components that constitute high density lipoprotein (HDL) in blood (see the specification, paragraph 0002). Applicants have demonstrated the effects of PON on diseases resulting from cerebral ischemic reperfusion and those resulting from cerebral infarction.

Specifically, Applicants have demonstrated in Experimental Examples 4-6 that PON produces the effects of improving prognosis, neurological symptoms and motor function on disorders resulting from ischemic reperfusion in a middle cerebral artery ischemia reperfusion model. Applicants have also demonstrated in Experimental Example 4 that PON produces a significantly higher suppression effect against cerebral infarction than the control group in the rat model of cerebral infarction (at 10 mg/mL/kg, intravenous administration

from tail). Claim 28 relates to such an effect of PON on a disease resulting from cerebral infarction.

In rejecting Claim 28 and its dependent Claims 29-38, the Office Action states that "Bisgaier teaches a method for treating and preventing ischemic reperfusion injury comprising administering effective amounts of PON . . . in combination with glycerols . . ., wherein the injury is to the brain, or is cerebral (0016)." At paragraph 0016, however, Bisgaier et al. merely mentions damages from ischemic reperfusion and does not refer to diseases resulting from cerebral infarction. Bisgaier et al. generally states that "[t]he methods and compositions of the invention can be useful in any context where treatment, reduction or protection from ischemic reperfusion injury might be useful," and that "the methods and compositions of the invention can protect the muscle and organs such as, for example, the heart, liver, kidney, brain, lung, spleen and steroidogenic organs . . . from damage as a result of ischemia reperfusion injury" (paragraph 0016). As such, the reference does not provide any descriptions or experimental results that suggest effectiveness of PON on a disorder resulting from cerebral infarction.

More specifically, Bisgaier et al. describes the effects of apolipoprotein (ETC-216) in the isolated ischemic rabbit heart (see 6.1. Example 1) and in the animal model of reperfusion of myocardial ischemia (6.2. Example 2 to 6.4 Example 4). However, the reference provides no experimental results demonstrating the effectiveness of ETC-216 for cerebral infarction. Bisgaier et al. also fails to provide experimental data supporting the effectiveness of lecithin cholesterol acyltransferase (LCAT) or PON for treatment of cerebral infarction in an animal model or in other ischemic reperfusion models (e.g., an animal model of myocardial ischemia). Further, nothing in Bisgaier et al. suggests that a common mode of action can be expected among the treatments using apolipoprotein, PON, and LCAT for a disorder resulting from ischemia reperfusion.

In addition, Bisgaier et al. does not suggest that a substance having an antioxidant action is expected to have effects on the treatment of cerebral infarction. It has been reported that substances having an antioxidant activity are ineffective in an animal experimental model or in clinical trials for prophylactic and therapeutic treatments of cerebral infarction (see Appendices A, B and C).

Appendix A: Salom et al., "Single-dose ebselen does not afford sustained neuroprotection to rats subjected to severe focal cerebral ischemia." *European Journal of Pharmacology* 495 (2004): 55-62.

Appendix B: Rossato et al., "Ebselen blocks the quinolic acid-induced production of thiobarbituric acid reactive species but does not prevent the behavioral alterations produced by intra-striatal quinolinic acid administration in the rat." *Neuroscience Letters* 318 (2001): 137-140.

Appendix C: The RANTTAS Investiragors, "A Randomized Trial of Tirilazad Mesylate in Patients With Acute Stroke (RANTTS)." *Stroke* 27.9 (1996): 1453-1458.

Specifically, Salom et al. states that "single-dose administration of ebselen does not reduce the size of brain infarcts" (see Abstract and page 61, left column, last paragraph). Rossato et al. states that ebselen does not alter QA-induced behavioral effects (see Abstract). The RANTTAS Investigators have examined whether tirilazad mesylate improves functional outcome after acute human stroke, and concluded that "[t]hese observations suggest that tirilazad . . . does not improve overall functional outcome" (page 1453, right column, "Conclusions" section). These articles show that ebselen and tirilazad mesylate having an antioxidant activity are ineffective in an animal experimental model or in clinical trials for prophylactic and therapeutic treatments of cerebral infarction. Therefore, Applicants respectfully submit that, based on the descriptions in the articles, the antioxidant substances

cannot be expected to have effects on a disorder resulting from ischemic reperfusion such as cerebral infarction. Therefore, the subject matter of Claim 28 is believed to be distinguishable from Bisgaier et al.

Welch et al. relates to a method for identifying small molecules that modulate premature translation termination and nonsense mediated mRNA decay. Welch et al. is simply cited for its reference to CHAPS and cannot cure the deficiencies of Bisgaier et al..

For the foregoing reasons, Claim 28 is believed to be allowable. Furthermore, since Claims 29-38 depend from Claim 28, substantially the same arguments set forth above also apply to these dependent claims. Hence, Claims 29-38 are believed to be allowable as well.

In view of the amendments and discussions presented above, Applicants respectfully submit that the present application is in condition for allowance, and an early action favorable to that effect is earnestly solicited.

Respectfully submitted,

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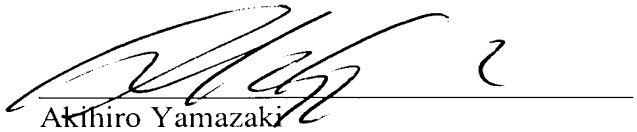

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